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Name

October 2, 2002
Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of: John C. Hiserodt

Serial No.: 09/162,648

Filing Date: September 29, 1998

For: CANCER IMMUNOTHERAPY USING ALLOSTIMULATED CELLS IN A MULTIPLE SEQUENTIAL IMPLANTATION STRATEGY

Art Unit: 1633

Examiner: Shin-Lin Chen, Ph.D.

DECLARATION UNDER 37 CFR § 1.132
BY JOHN C. HISERODT

I, John Hiserodt, do hereby declare:

1. I am the inventor of the subject matter claimed in this patent application. I have read the specification and the claims as currently pending.

2. I understand the Patent Office has questioned the relationship between this application and PCT publication WO 98/16238. The PCT publication has been issued in the U.S. as Patent 6,207,147 (March 27, 2001). World-wide rights to the technology in U.S. 6,207,147, and to the technology described in the Granger patents (U.S. 5,837,233 and 6,136,306) are owned by the University of California, and licensed exclusively to Meyer Pharmaceuticals LLC.

3. I was previously on faculty of the University of California at Irvine, where I did research in conjunction with Dr. Gale A. Granger. Work done in Dr. Granger's group at UCI lead to the filing of the application which was published as WO 98/16238, and issued as U.S. 6,207,147. The disclosure is entitled, "Cancer Immunotherapy using Tumor Cells Combined with Mixed Lymphocytes".

4. I subsequently became a senior scientist at Meyer Pharmaceuticals, where the discovery claimed in the present patent application was made by me, and technicians working under my supervision.

5. The two inventions are different in their nature and practice. The intention described and claimed in U.S. 6,207,147 is a vaccine containing both alloactivated lymphocytes and tumor antigen. The vaccine is administered at a convenient site *away from the primary tumor.* Like other vaccines, it may be administered in multiple doses to boost or enhance the immunological response.

6. In contrast, the invention described and claimed in the present application is an improvement taught in U.S. Patents 5,837,233 and 6,136,306. This is a method for treating cancer in which alloactivated cells are administered *directly into the tumor bed.* The composition does not require tumor antigen. It elicits a host response against itself, and then against residual tumor antigen that is present at the tumor site after removing the tumor. The Granger patents show that a single administration of the implant is fully effective to elicit an immune response and provide considerable therapeutic benefit to patients treated in the clinical trials.

7. The present application teaches that administering a second alloactivated cell population into the tumor site at a subsequent time has a surprisingly improved beneficial effect. Even though the first administration is sufficient to elicit a therapeutic anti-tumor immunological response, the second administration provides unexpected additional benefit. The second administration turns out to be extremely effective in augmenting regression of the tumor and preventing metastases.

8. Contrary to standard practice and belief, this invention means that it is actually *beneficial* to leave tumor in the patient, in order to provide bystander antigen for the second administration of alloactivated cells.

9. This practice is very different from the practice described in the vaccine patent (U.S. 6,207,147). Tumor antigen in the vaccine patent is *part of the composition*, typically in the form of isolated antigen or inactivated tumor cells from any source. There is no need for the treating clinician to leave tumor cells in the patient. Furthermore, leaving tumor cells in the patient would not contribute any known benefit, because the alloactivated cells and tumor antigen are being administered at a different site.

10. I hereby declare that all statements made in this Declaration of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

10-01-02
Date

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